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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
09/113,924	07/09/98	BRIGSTOCK	D 08766/003002

HM12/0315

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EXAMINER	
SPECTOR, L	
ART UNIT	PAPER NUMBER
1647	18

DATE MAILED: 03/15/01

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 2/2/01

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-7 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-7 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

-- SEE OFFICE ACTION ON THE FOLLOWING PAGES --

Part III: Detailed Office Action

Notice: **Effective June 18, 2000**, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit **1647**.

The request filed on 2/2/01 for a Continued Prosecution Application (CPA) under 37 C.F.R. § 1.53(d) based on parent application number 09/113924 is acceptable and a CPA has been established. An action on the CPA follows.

Claims 1-7 are pending and under consideration.

All prior art rejections under 35 U.S.C. §102 and §103 set forth in the previous Office Action are withdrawn in view of applicants amendments to the claims.

Objections to the Claims:

Claim 7 is objected to under 37 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Rejections under 35 U.S.C. §112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification discloses HBGF, which is a protein which is a fragment of Connective Tissue Growth Factor (CTGF), a longer protein. CTGF was itself isolated by virtue of antigenic cross-reactivity with another protein, platelet derived growth factor (PDGF). The claims have been amended to require that the claimed antibodies not be "reactive with CTGF or with platelet derived growth factor."

Because HBGF is a sub-fragment of a longer protein, (to which antibodies are known in the prior art, see previous Office Action), it is not predictable that the mere act of cleaving the HBGF from the longer precursor, CTGF, would produce novel epitopes such that antibodies could be made, without undue experimentation, to HBGF that would not be cross-reactive with CTGF. The prior art does not recognize, as argued by applicants, that such cleavage would produce epitopes "substantially different from those presented by CTGF" (page 5, first paragraph of the response), nor that an anti-CTGF antibody "would not reasonably be expected to be "specifically reactive with HBGF as claimed." Applicants argument that it would not be predictable that antibodies to HBGF would cross-react with CTGF, let alone with PDGF, because the epitopes presented by HBGF would be expected to be substantially different from those presented by CTGF has been fully considered but is not deemed persuasive antibodies to PDGF ***would*** reasonably be expected to be reactive with HBGF. Applicants argument that antibodies raised to isolated peptides would not predictably be expected to be reactive with a longer protein is contrary to the state of the art as evidenced by Lerner, Advances in Immunology 36:1-44, Academic Press 1984, which teaches exactly the opposite; see for example pages 7-11, for a discussion of anti-peptide antibodies, page 27 which discusses results in which 16 out of 21 monoclonal antibodies raised against isolated peptides from influenza virus recognized both the peptide they were raised against and the whole virus, and page 33, which states that "sufficient structural information is contained in peptides as small as 13 amino acids residues to induce protein reactive antibodies at a high frequency." Additionally, Lerner, Nature 299:592, 1982,

teaches that protein fragments are useful as antigens for the production of antibodies. Lerner teaches that the use of fragments for the production of antibodies allows production of antibodies reactive to a wider variety of antigenic determinants than can be attained using whole protein (see, e.g. last sentence of paragraph bridging pages 593-594). At page 596, Lerner teaches "The minimum size of the peptide chosen is important and should be larger than six amino acids. We generally synthesize peptides of 15 amino acids. Considerably larger peptides have also proved useful but do not offer any advantage..."

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

In this case, the nature of the invention is antibodies to a protein which is disclosed to be a fragment of a larger protein, and the prior art clearly teaches that one would expect antibodies to the fragment to bind to the whole. The level of skill in the art is high. The level of predictability (as taught by the prior art) is that one would predict cross reactivity, and the ability to generate antibodies within the metes and bounds of the claim would be considered to be unpredictable. There are no working examples of antibodies within the metes and bounds of the claims. Although the claims are limited to antibodies which do not react with PDGF or CTGF, given the teachings of the prior art discussed above, the Examiner concludes that it would require undue experimentation to find antibodies within the metes and bounds of the claims, and further, that it is not predictable that such could be obtained at all. Accordingly, the specification does not enable the claims as currently amended.

Advisory Information:

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 37 C.F.R. § 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 37 C.F.R. § 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 8:00 A.M. to 4:30 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Paula Hutzell, Ph.D, can be reached at (703)308-4310.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Group 1800 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to (703) 305-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. **Please** advise the Examiner at the telephone number above when an informal fax is being transmitted.

Lorraine Spector, Ph.D.
Primary Examiner

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